REMARKS

After entry of this amendment, claims 1-34 are pending, of which claims 11-20, and 27-31 are withdrawn. The claims have been amended without disclaimer or prejudice and find support *inter alia* in the original claims. Claims 4-6 and 21-24 have been amended without disclaimer or prejudice cancelling non-elected subject matter as requested by the Examiner. Because the amendments to claims 4, 5, 21, and 23 are requested by the Examiner and based on an election of species, Applicants reserve all rights to rejoinder and examination of the non-elected species upon allowance of the generic claims or the claims directed to the elected species. 37 CFR § 1.141; MPEP § 809.02(a). The amendments to claims 6, 22, and 24 additionally find support in the specification at page 14, lines 4-10. The subject matter of claim 2 has been incorporated into claim 1 and finds support in original claims 1 and 2 and in the specification at page 5, lines 7-31. Accordingly, claim 2 has been cancelled without disclaimer or prejudice. Claims 1, 3, 4, 10, 23, 25, and 26 have been amended without disclaimer or prejudice for clarification and/or for proper dependency and antecedent basis. Support for the amendments to claims 1, 3, 4, 10, 23, 25, and 26 is found in the original claims and in the specification at page 5, lines 25-26. New claims 32 and 33 find support in original claims 1, 4, 5, and 10, and in the specification at page 12, line 36 through page 20, line 15. New claim 34 finds support in original claim 10. No new matter has been added. New claims 32-34 are dependent from claim 1, directly or indirectly, and as such are consistent with elected Group I drawn to a process for preparing transformed plant cells or organisms.

The specification has been amended to include a paragraph directed to the related applications already of record, to delete an embedded hyperlink or other browser-executable code, and to correct a typographical error. No new matter has been added.

Objections To The Specification and The Claims

In light of the amendments, the objections to the specification and to the claims are believed to be rendered moot. Reconsideration and withdrawal of the objections to the specification and to the claims are respectfully requested.

Claim Rejections – 35 USC § 112, second paragraph

The Examiner rejects claim 1 as indefinite for reciting "marker protein capable of causing directly or indirectly a toxic effect" and "an expression cassette ...." Claim 1 has been amended without prejudice or disclaimer for clarification. In light of the amendments to claim 1, these rejections are believed to be rendered moot.

The Examiner also rejects claim 1 as indefinite for reciting "double-stranded marker protein ribonucleic acid sequence." Applicants respectfully disagree. This term is described throughout the specification for example, at page 21, lines 39-45, and at page 23, lines 7-8, 39-44 and refers to a double-stranded ribonucleic acid sequence of a marker protein. Reconsideration and withdrawal of the rejection is respectfully requested.

The Examiner rejects claim 2 as indefinite for reciting "capable of converting." The subject matter of claim 2 has been incorporated into claim 1 and claim 2 has been cancelled without disclaimer or prejudice. Amended claim 1 does not recite "capable of converting." The Examiner also rejects claim 2 as indefinite for reciting "toxic." Applicants respectfully disagree. The term is described in the specification at page 11, lines 41-46 through page 12, lines 1-4; the standard being toxicity sufficient to carry out selection of transformed cells, thus allowing discrimination between transformed and untransformed cells. Reconsideration and withdrawal of this rejection is respectfully requested.

Claims 10 and 26 were rejected as indefinite for reciting "preferably non-plant," "such as," and "further comprising." Claims 10 and 26 have been amended without disclaimer or prejudice. In light of the amendments, these rejections are believed to be rendered moot. Reconsideration and withdrawal of this rejection is respectfully requested.

Claims 22 and 24 were rejected for reciting a GenBank Accession No. In light of the amendments, this rejection is believed to be rendered moot. Furthermore, claim 6 also recites a GenBank Accession No. and has similarly been amended without disclaimer or prejudice.

The Examiner also rejected claim 26 as indefinite for reciting "said nucleic acid." Claim 26 has been amended without disclaimer or prejudice for clarification. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejections Under 35 USC § 112, first paragraph

Claims 1-5, 7-10, 21, 23, and 25-26 are rejected under 35 U.S.C. 112, first paragraph, for allegedly failing to comply with the written description requirement and for lack of enabling disclosure. Applicants respectfully disagree, and traverse the rejections of the following reasons.

Written Description

The Examiner alleges that the specification does not describe other species in the claimed genus of marker proteins except for those listed in claim 4. Applicants respectfully disagree with the Examiner's characterization. Claim 4 which depends from claims 2 or 3 does not recite marker proteins but rather provides a list of substance X to be used in a process for preparing transformed plant cells, wherein a marker protein is capable of transforming directly or indirectly a substance X. Rather claim 5 recites seventeen different marker proteins which can be used in the process of claim 1.

The Examiner also alleges that the specification fails to correlate the conserved structures of the marker proteins to function, and fails to present representative number of species of the claimed genus of marker proteins. Applicants strongly disagree.

The applicable test for written description is stated in the "Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, 1, Written Description Requirements" 66 Fed. Reg. 1099, 1106 (Jan. 5, 2001). As there indicated, the written description requirement for a claimed genus can be satisfied in a number of alternative ways, such as through sufficient description of a representative number of species by actual reduction to practice, by disclosure of relevant identifying characteristics, by functional characteristics coupled with known or disclosed correlation between function and structure, or by a combination of such identifying characteristics. Furthermore, written description under 35 U.S.C. § 112, first paragraph, is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been

presented by the examiner to rebut the presumption. *In re Marzocchi*, 439 F.2d 220, 224 (CCPA 1971); MPEP § 2163.04.

In the present application, the Patent and Trademark Office (PTO) has not provided sufficient evidence to rebut the presumption of adequacy of a description to a process using marker proteins and double-stranded marker protein ribonucleic acids. In *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997) cited by the Examiner, the Federal Circuit held that a "description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs..." In the present application, the Examiner simply stated that the specification does not describe other species except those of claim 4 and that those species belong to one of the subgenera of the genus. The Examiner has not provided any explanations regarding the subgenera. This statement does not provide any evidence which would be sufficient to rebut the presumption of adequacy of a description of the process claimed. As mentioned above, claim 5 recites seventeen marker proteins which can be used in the process; furthermore claim 6 provides 25 sequences identified by GenBank Accession number and 24 sequences identified by SEQ ID NO that can be used in the process. Seventeen marker proteins and at least 24 actual sequences is clearly a "representative" number of species of the genus and the Examiner has not provided reasons why it is not.

The Examiner also alleges that the specification fails to correlate the conserved structures of the marker proteins to the function, citing to *Regents v. Lilly*. Applicants respectfully disagree. For a "function" such as toxicity, the function is not achieved based on a common structure (toxicity is achieved by different mechanisms). Furthermore, the specification clearly describes the correlation between each marker protein and the corresponding substance X which the marker protein converts (see specification pages 12-20 in items a) through n)). This is a case where a representative number of species is a more relevant manner of supplying written description. Thus, given the representative number of species described (*i.e.* seventeen marker proteins, at least 25 sequences identified by GenBank Accession number, and at least 24 sequences described by SEQ ID NO), a correlation between structure and function is not required under the applicable test for written description.

Because each embodiment within a claim need not be disclosed, the specification, which describes at least seventeen marker proteins and at least 24 actual sequences, provides a representative number of species under the standard of *Regents v. Lilly*. See *In re Angstadt*, 537 F.2d 498 (CCPA 1976) (holding that there has never been a requirement that every species encompassed by a claim must be disclosed or exemplified in a working example). Moreover, the claims are directed to a method of using the marker proteins and not to marker proteins *per se*.

Separate consideration is requested as to claims 32 and 33, which recites a method of using specific marker proteins and the substances X that the marker proteins are capable of converting.

For these reasons, it is submitted that the specification provides adequate written description and that the PTO has not presented a *prima facie* case showing a lack of sufficient written description for the claimed process. Reconsideration and withdrawal of this rejection is respectfully requested.

Enablement

The Examiner argues that the specification allegedly does not provide any guidance to practice the invention using marker proteins with different modes of action from the one of codA and does not provide guidance on how to practice the invention without using 5-fluorocytosine. Applicants respectfully disagree.

As mentioned above, the specification provides detailed description and guidance regarding at least seventeen specific marker proteins which can be used in the claimed process, the corresponding substance X which each marker protein converts either directly or indirectly, the specific reactions involved, and sequences identified by GenBank Accession number or by SEQ ID NO. See specification at pages 12-20 in items a) through n). The specification also describes in detail the relationship between the marker protein and the corresponding substance X which the marker protein converts and the associated reaction as described at pages 12-20. Furthermore, because of the recognition in the art of the relationship between the marker proteins and their corresponding substance X, as also described in the specification, only routine experimentation would be needed to determine a suitable concentration of substance X for

selection. The marker proteins and their substrates are not novel *per se* and are not claimed as such. Since their function is known in the art, there is no reason to require description of that function in the present application. The law is clear what a specification need not describe, and preferably omits information already known in the art.

Separate consideration is requested as to claims 32 and 33, which recites a method using specific marker proteins and the corresponding substance X that the marker proteins are capable of converting as described in the specification at pages 12-20 in items a) through n).

The specification provides a detailed description including working examples on how to prepare transgenic expression vectors for expressing double-stranded marker protein ribonucleic acid (Examples 1-2), how to prepare transgenic plants with the expression vector and marker protein (Examples 4-6), and how to carry out and analyze the claimed selection method (Examples 7-11). Furthermore, as discussed above, the specification provides at least seventeen examples of specific marker proteins with the corresponding substance X which each marker protein converts either directly or indirectly that would lead a skilled person to conclude that the method as claimed is operable with any marker protein. In view of the detailed description, guidance, working examples, and high level of skill, the specification enables the full scope of the claims without undue experimentation. On these facts, an analysis under *In re Wands* supports enablement. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (found that routine screening of hybridomas was not "undue experimentation;" the involved experimentation can be considerable, so long as "routine").

Furthermore, each embodiment need not be supported by working examples. *In re Angstadt* , 537 F.2d 498 (CCPA 1976) (holding that there has never been a requirement that every species encompassed by a claim must be disclosed or exemplified in a working example). For the reasons above, the record supports enablement. Reconsideration and withdrawal of this rejection is respectfully requested.

Rejections Under 35 USC § 103(a)

Claims 1-10 and 21-26 are rejected as being obvious under 35 U.S.C. § 103(a) over Maliga *et al.* (WO 01/21768, hereinafter "Maliga") in view of Smith *et al.* (Nature; hereinafter

"Smith") and Applicants' specification. Applicants respectfully disagree and traverse the rejection.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. See MPEP § 2143.03.

The Examiner argues that Maliga teaches that plant seedlings expressing codA are sensitive to 5FC and seedlings lacking codA (by deletion due to expression of site-specific recombinase) could be readily identified by 5FC resistance (citing to page 34 of Maliga). The Examiner acknowledges that Maliga does not teach suppression of codA by using a dsRNA gene silencing construct targeting the codA gene and does not teach using positive selection in combination with negative selection. The Examiner relies on Smith for teaching a DNA construct that produces a hairpin loop type dsRNA with functional (*i.e.* spliceable) intron as a spacer. The Examiner further relies on Applicants disclosure for showing that positive selection markers and negative selection markers are known in the art. Applicants respectfully disagree with the Examiner's characterization of these references and their relevance to the claimed process.

Maliga teaches a site specific recombination method to remove heterologous sequences from the plastid genome using two constructs, one with a nucleic acid encoding a protein having excision activity (see Maliga page 3, lines 6-8, 13-35). Maliga also describes a construct which "express cytosine deaminase at sufficiently high levels to be useful to implement a negative selection scheme." (Maliga at page 34, lines 21-23). Maliga explains that they found that seedlings and plant tissues expressing codA were sensitive to 5FC and that those lacking codA could be readily identified by 5 FC resistance (Maliga at page 34, lines 17-20). Thus, Maliga describes using expression of codA for selection. In contrast to Maliga, the claimed selection method relates to a process for preparing transformed plant cells or organisms using a marker protein and a double-stranded marker protein ribonucleic acid sequence which reduces the expression of the marker protein. The method taught by Maliga does not teach or suggest reducing expression of the marker protein in any way, as also acknowledged by the Examiner (see Office Action, at page 13, last paragraph). Smith does not remedy the deficiencies of Maliga. Smith describes gene constructs encoding intron-spliced RNA with a hairpin structure

that can induce post-transcriptional gene silencing. Smith does not teach any selection method or the use of their gene construct for reducing expression of a marker protein in a selection method.

The Examiner argues that because of the recognition of those of ordinary of skill in the art of the value of discovering new or alternative selection markers for plant transformation, the present invention would be obvious. Applicants respectfully disagree. This alleged motivation lacks specificity to support a legal conclusion of obviousness. See *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 at 1741 (2007) (holding that "there must be some articulated reasoning with some rational underpinning to support a legal conclusion of obviousness."). *KSR* still requires some reason one would have combined Maliga and Smith. *Id.* (holding that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. . . it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does."). The alleged recognition of one of ordinary skill in the art of the value of discovering new selection markers for plant transformation does not provide a reason that would have prompted a person of ordinary skill in the relevant field to combine the hairpin structure of Smith with the teaching of a site specific recombination method to remove heterologous sequences from the plastid genome of Maliga. Specifically, the present claims are not directed to new or alternative selection markers for plant transformation, but rather to a process of preparing transformed plant cells or organisms using known marker proteins in a new and unobvious way. Thus, the motivation to combine suggested by the Examiner – identification of new selection markers – would be met by the primary reference alone, and provides no motivation to combine the disparate teachings of Maliga and Smith. Applicants claimed process requires reducing the expression of the marker protein in the transformed cells, which is opposite to the teaching in Maliga requiring expression of the marker protein for selection. Based on a teaching requiring expression a marker protein for selection in a site specific recombination method to remove heterologous sequences from the plastid genome, one of ordinary skill in the art would not look to a reference disclosing gene silencing.

Furthermore, if the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references normally do not render the claims obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959) (The court reversed the obviousness rejection holding the "suggested combination of references would require a substantial reconstruction and redesign of the elements shown in [the primary reference] as well as a change in the basic principle under which the [primary reference] construction was designed to operate." 270 F.2d at 813, 123 USPQ at 352.). MPEP § 2143.02 VI. The proposed modification to Maliga suggested by the Examiner requires a "substantial reconstruction and redesign" of elements and changes the principle under which Maliga operates, from the site specific recombination method to remove heterologous sequences from the plastid genome expressing a marker protein taught in Maliga to the claimed selection process for preparing transformed plant cells or organisms using a marker protein and a double-stranded marker protein ribonucleic acid sequence which reduces the expression of the marker protein. Maliga describes a site specific recombination method to remove heterologous sequences from the plastid genome using two constructs, with a specific construct where the marker gene is flanked by excision sites allowing for removal of the marker gene and site specific recombination (see Maliga, Summary of the invention pages 3-4). Maliga uses the selectable marker as the heterologous sequence to be removed in their method. The selection marker is used as a tool for determining that their method for removing heterologous sequences actually removes the desired sequence (see for example, Maliga, Example 1, pages 20-35). Modifying the method disclosed by Maliga, which requires expression of the marker protein, to the construct used in the claimed invention requiring reducing expression of a marker protein in the transformed cells, changes the basic principle under which the Maliga construct was designed to operate. Smith provides no motivation for changing the method of removing heterologous sequences disclosed by Maliga to a totally different manner of operation. Introducing the construct of Smith, *i.e.* a gene construct encoding an intron-spliced RNA with a hairpin structure for post-transcriptional gene silencing, into the method of Maliga would render it inoperable. Thus, Maliga and Smith are not combinable.

Additionally, the Examiner argues that the present specification discloses that negative and positive selection markers are known in the art. Whether or not positive and/or negative

selection markers are known, such a disclosure in combination with Maliga and Smith still does not teach or suggest the specific steps of the selection method as claimed.

The Examiner also alleges that one of ordinary skill in the art would modify the method by adding a positive selection marker based on Applicants teaching of known markers and would be motivated to do so based on double selection being more effective to select true transformants. The Examiner has improperly used hindsight based on Applicants' own disclosure for the teaching of a double selection. As acknowledged by the Examiner, Maliga does not teach or suggest using positive selection in combination with negative selection and neither does Smith. Even if positive and/or negative selection markers are known, a method using known marker proteins in a new and nonobvious way as recited in the claims is not taught or suggested in Maliga and Smith or by the knowledge of either a positive or a negative marker.

In summary, Maliga and Smith, alone or in combination, do not disclose or teach all the limitations of the present claims. Furthermore, the proposed modification to Maliga suggested by the Examiner requires a "substantial reconstruction and redesign" of elements and changes the principle under which Maliga operates. Maliga and Smith are not combinable; the introduction of the hairpin structure of Smith into a site specific recombination method to remove heterologous sequences from the plastid genome using two constructs as taught in Maliga would be inoperable. Therefore, Maliga and Smith, alone or in combination, do not render obvious the subject matter of independent claim 1 or the claims dependent therefrom. *See In re Fine*, 837 F.2d 1071, 1076 (Fed. Cir. 1988) (holding that if an independent claim is nonobvious then any claim dependent therefrom is nonobvious).

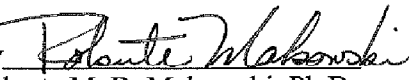
Reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the amendments and the reasons presented above, reconsideration of the rejections and allowance of the claims is respectfully requested. If any outstanding issues remain, the Examiner is invited to telephone the undersigned at the number given below.

Accompanying this response is a petition for a three-month extension of time to and including November 30, 2007 to respond to the Office Action mailed May 31, 2007 with the required fee authorization. No further fee is believed due. However, if any additional fee is due, the Director is hereby authorized to charge our Deposit Account No. 03-2775, under Order No. 12810-00057-US from which the undersigned is authorized to draw.

Respectfully submitted,

By 

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